

### AMENDMENTS TO THE CLAIMS

Please amend the claims as follows:

#### LISTING OF CLAIMS:

Claim 1 (currently amended). An isolated nucleic acid having the sequence of SEQ ID NO:1 or a nucleic acid that encodes a polypeptide having the sequence of SEQ ID NO:7 ~~sequence complementary to SEQ ID NO.: 1, wherein the sequence of SEQ ID NO.: 1 encodes a *C. elegans* chloride intracellular channel protein.~~

Claim 2 (previously presented). The nucleic acid of claim 1, wherein the nucleic acid is a DNA, RNA or a PNA.

Claim 3 (previously presented). The nucleic acid of claim 2, wherein the nucleic acid is single stranded or double stranded.

Claim 4 (currently amended). An isolated nucleic acid which encodes a mutant chloride intracellular channel protein whose amino acid sequence is identical to SEQ ID NO:7, except for the presence of one mutation or polymorphism encoding a mutant EXC-4 ~~protein, wherein the isolated nucleic acid has a sequence identical to the sequence of SEQ ID NO.: 1, except for the presence of one or more missense mutations, nonsense mutations, point mutations, substitutions, deletions, insertions, polymorphisms, or rearrangements, and wherein the isolated nucleic acid encodes for a mutant chloride intracellular channel protein.~~

Claim 5 (previously presented). A recombinant expression vector comprising the isolated nucleic acid of claim 1.

Claim 6 (previously presented). A recombinant expression vector comprising the isolated nucleic acid of claim 4.

Claim 7 (previously presented). A host cell comprising the recombinant vector of claim 5.

Claim 8 (previously presented). A host cell comprising the recombinant vector of claim 6.

Claim 9 (previously presented). A method of generating an EXC-4 protein, comprising the steps of:

- (a) introducing the nucleic acid of claim 1 into a host cell;
- (b) culturing the host cell under conditions allowing expression of the nucleic acid; and
- (c) recovering the EXC-4 protein.

Claim 10 (previously presented). A method of generating a mutant EXC-4 protein, comprising the steps of:

- (a) introducing the nucleic acid of claim 4 into a host cell;

(b) culturing the host cell under conditions allowing expression of the nucleic acid; and

(c) recovering the mutant EXC-4 protein.

Claim 11 (withdrawn). A composition comprising an anti-EXC-4 antibody or an antigen binding fragment thereof, wherein the antibody or antibody fragment specifically binds to all or a portion of the amino acid residues encoded by SEQ ID NO.: 1.

Claim 12 (withdrawn). The composition of claim 11, wherein the antibody is a monoclonal antibody.

Claim 13 (withdrawn). The composition of claim 11, wherein the antibody is a polyclonal antibody.

Claim 14 (withdrawn). The composition of claim 11, wherein the antibody is a humanized antibody.

Claim 15 (withdrawn). The composition of claim 11, wherein the antibody is a chimeric antibody.

Claim 16 (withdrawn). The composition of claim 11, wherein the antibody is a single chain antibody.

Claim 17 (withdrawn). The composition of claim 11, where the antigen binding fragment is a Fab, F(ab1)2 or Fv fragment.

Claim 18 (withdrawn). The composition of claim 11, further comprising a detectable label.

Claim 19 (withdrawn). The composition of claim 18, wherein the detectable label is an enzymatic label, a fluorescent label, a chemiluminescent label, a bioluminescent label or a radioactive label.

Claim 20 (withdrawn). A method of identifying a putative agent that inhibits CLIC activity, the method comprising the steps of:

(a) contacting a *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell with an agent of interest, wherein the *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell comprises a wild-type exc-4 allele;

(b) measuring the resulting levels of EXC-4 activity in the developing *C. elegans* embryo or isolated *C. elegans* excretory cell; and

(c) comparing the measured levels of EXC-4 activity in the treated *C. elegans* embryos or isolated excretory cells to levels of EXC-4 activity in a suitable control, wherein a reduced level of EXC-4 activity relative to the suitable control indicates that the agent of interest is a putative agent that inhibits CLIC activity.

Claim 21 (withdrawn). The method of claim 20, wherein the agent of interest is a peptide, a nucleic acid, an antibody, a drug, a compound, a molecule, or a dominant-negative antagonist.

Claim 22 (withdrawn). The method of claim 20, wherein the agent of interest is one of indanyloxyacetic acid-94, N-ethylmaleimide, or glutathione.

Claim 23 (withdrawn). A method of identifying a putative agent that inhibits CLIC expression or function, the method comprising the steps of:

(a) contacting a *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell with an agent of interest, wherein the *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell comprises a wild-type exc-4 allele; and

(b) observing the resulting excretory cell phenotype of the developing *C. elegans* embryo or isolated *C. elegans* excretory cell, wherein an excretory cell phenotype characteristic of an exc-4 *C. elegans* mutant indicates that the agent of interest is a putative agent that inhibits CLIC expression or function.

Claim 24 (withdrawn). The method of claim 23, wherein the agent of interest is a peptide, a nucleic acid, an antibody, a drug, a compound, a molecule, or a dominant-negative antagonist.

Claim 25 (withdrawn). The method of claim 24, wherein the agent of interest is a candidate agent for inhibiting angiogenesis in humans.

Claim 26 (withdrawn). The method of claim 23, wherein the agent of interest is one of indanyloxyacetic acid-94, N-ethylmaleimide, or glutathione.

Claim 27 (withdrawn). A method of identifying a putative agent that inhibits CLIC expression, the method comprising the steps of:

(a) contacting a *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell with an agent of interest, wherein the *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell comprises a wild-type exc-4 allele; and

(b) measuring levels of expression of the exc-4 allele following contact with the agent of interest, wherein a reduced level of exc-4 expression as compared to a suitable control indicates that the agent of interest is a putative agent that inhibits CLIC expression.

Claim 28 (withdrawn). The method of claim 27, wherein the agent of interest is a peptide, a nucleic acid, an antibody, a drug, a compound, a molecule, or a dominant-negative antagonist.

Claim 29 (withdrawn). The method of claim 28, wherein the agent of interest is a candidate agent for inhibiting angiogenesis in humans.

Claim 30 (withdrawn). The method of claim 27, wherein the agent of interest is one of indanyloxyacetic acid-94, N-ethylmaleimide, or glutathione.

Claim 31 (withdrawn). A method of determining whether a CLIC gene is involved in tubulogenesis, comprising the steps of:

(a) providing an embryonic exc-4 mutant of *C. elegans* or an isolated embryonic excretory cell derived from an exc-4 mutant of *C. elegans*;

(b) expressing a CLIC gene in the embryonic exc-4 mutant of *C. elegans* or isolated embryonic excretory cell derived from an exc-4 mutant of *C. elegans*, wherein the CLIC gene is operatively linked to a *C. elegans* promoter; and

(c) observing the resulting excretory cell phenotype of the developing embryonic exc-4 mutant of *C. elegans* or isolated embryonic excretory cell derived from an exc-4 mutant of *C. elegans*, wherein an excretory cell phenotype characteristic of wild-type exc-4 expression indicates that the CLIC gene is involved in tubulogenesis.

Claim 32 (withdrawn). The method of claim 31, wherein the CLIC gene is from a human.

Claim 33 (withdrawn). The method of claim 32, wherein the human CLIC gene is one of human CLIC 1, human CLIC 2, human CLIC 3, human CLIC 4, human CLIC 5, or human CLIC 6.

Claim 34 (withdrawn). A method of identifying a putative agent that inhibits CLIC expression or function, the method comprising the steps of:

(a) providing a *C. elegans* embryo or isolated *C. elegans* embryonic excretory cell, wherein the *C. elegans* embryo is an *exc-4* mutant or the isolated *C. elegans* embryonic excretory cell is derived from an *exc-4* mutant;

(b) expressing a CLIC gene in the embryonic *exc-4* mutant of *C. elegans* or isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans*, wherein the CLIC gene is operatively linked to a *C. elegans* promoter and expression of the CLIC gene rescues the *exc-4* mutant phenotype;

(c) contacting the embryonic *exc-4* mutant of *C. elegans* expressing the CLIC gene or isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans* expressing the CLIC gene with an agent of interest; and

(d) observing the resulting excretory cell phenotype of the developing embryonic *exc-4* mutant of *C. elegans* or isolated embryonic excretory cell derived from an *exc-4* mutant of *C. elegans*, wherein a reversionary excretory cell phenotype characteristic of an *exc-4* *C. elegans* mutant indicates that the agent of interest is a putative agent that inhibits CLIC expression or function.

Claim 35 (withdrawn). The method of claim 34, wherein the CLIC gene is from a human.

Claim 36 (withdrawn). The method of claim 35, wherein the human CLIC gene is one of human CLIC 1, human CLIC 2, human CLIC 3, human CLIC 4, human CLIC 5, or human CLIC 6.



Claim 37 (withdrawn). The method of claim 34, wherein the agent of interest is a peptide, a nucleic acid, an antibody, a drug, a compound, a molecule, or a dominant-negative antagonist.

Claim 38 (withdrawn). The method of claim 37, wherein the agent of interest is a candidate agent for inhibiting angiogenesis in humans.

Claim 39 (withdrawn). The method of claim 34, wherein the agent of interest is one of indanyloxyacetic acid-94, N-ethylmaleimide, or glutathione.

Claim 40 (currently amended). The isolated nucleic acid ~~encoding a mutant EXC-4 protein of claim 4, which encodes a mutant polypeptide wherein the isolated nucleic acid has a sequence of an exc-4 mutant allele~~ selected elected from the group consisting of rh133, n561 and n2400.

Claim 41 (new). The isolated nucleic acid sequence of claim 1 comprising the sequence of SEQ ID NO:1.

Claim 42 (new). An isolated nucleic acid sequence that is complementary to SEQ ID NO:1 or to a polynucleotide sequence that encodes SEQ ID NO:7.